CLAIMS

1. A nucleic acid construct comprising viral genomic nucleic acid, said viral genomic nucleic acid comprising at least two endogenousgene expression regulatory units which each comprise an endogenous promoter capable of expression in a mammalian cell, where the endogenous promoters of the units are active at the same phase in the viral life cycle of the virus the viral genomic nucleic acid is derived from, where:

(a) at least two of the endogenous gene expression regulatory units comprising promoters active at the same phase are each operably linked to a separate heterologous coding sequence inserted into the viral genomic nucleic acid; and

(b) the viral genomic nucleic acid is from 1 to 50 kb in length excluding the heterologous sequences inserted into it.

2. A nucleic acid construct according to claim 1, wherein the at least two endogenous promoters are switched on at the same point in the viral life cycle of the virus the genomic nucleic acid is derived from.

3. A nucleic acid construct according to claim 1, wherein the at least two endogenous gene expression regulatory units are either both/all from immediate early or both/all from early viral genes.

4. A nucleic acid construct according to claim 1, wherein the at least two endogenous gene expression regulatory units are different.

5. A nucleic acid construct according to claim 1, wherein the virus the viral genomic nucleic acid is derived from is selected from the group consisting of a DNA virus and an RNA virus.

6. A nucleic acid construct according to claim 5, wherein the DNA virus is a double stranded DNA virus selected from a herpesvirus and an adeno associated virus (AAV).

7. A nucleic acid construct according to claim 6, wherein the herpesvirus is selected from the group consisting of a herpes simplex virus (HSV), a cytomegalovirus (CMV) and an Epstein Barr virus (EBV).

8. A nucleic acid construct according to claim 7, wherein the HSV is selected from the group consisting of HSV-1 and HSV-2.

9. A nucleic acid construct according to claim 7, wherein the viral genomic nucleic acid is derived from a herpes simplex virus and the at least two endogenous gene expression regulatory units each comprise an endogenous promoter selected from the group consisting of the ICP0, ICP4, ICP22 and ICP27 gene promoters.

10. A nucleic acid construct according to claim 7, wherein the viral genomic nucleic acid is derived from a herpes simplex virus and the two endogenous promoters of the at least two gene expression regulatory units are HSV tegument protein gene promoters.

11. A nucleic acid construct according to claim 7, wherein the viral genomic nucleic acid is from human cytomegalovirus and the endogenous promoters of the at least two gene expression regulatory units are:

- at least two selected from the group consisting of the UL36, UL37 and UL38 gene promoters;
- the UL82 and UL83 gene promoters; or
- the UL122 and U123 gene promoters.

12. A nucleic acid construct according to claim 1, wherein all of the heterologous coding sequences expressed by the endogenous gene expression regulatory units are derived from the same organism.

13. A nucleic acid construct according to claim 1, wherein two or more of the heterologous coding sequences encode antigens.

14. A nucleic acid construct according to claim 1, wherein the antigens are antigens from a pathogen.

15. A nucleic acid construct according to claim 1, wherein some or all of the viral sequences, apart from the at least two endogenous gene expression regulatory units, which are present in the region of the viral genome corresponding to that between the 5' and 3' ends of the viral genomic nucleic acid in the construct are absent from the construct.

16. A nucleic acid construct according to claim 15, wherein the absent region comprises part or all of the intervening sequences between two of the adjacent endogenous gene expression regulatory units linked to heterologous coding sequences.

17. A nucleic acid construct according to claim 15, wherein the absent region corresponds to one or more of the genes present in the region of the viral genome other than those of the at least two endogenous gene expression regulatory units used to express the heterologous coding sequences.

18. A nucleic acid construct according to claim 15, wherein the viral genomic nucleic acid is from HSV-2 and the viral sequences have been removed from the construct by one or more of the following techniques:

(a) a partial digestion with a BstXI enzyme and then religation to remove sequences between ICP27 and ICP0;

(b) a complete digestion with a BspHI enzyme, followed by a partial digestion with a BsiWI enzyme and then religation to remove sequences adjacent to ICP22;

(c) a digestion with a SrfI enzyme and then religation to remove sequences between ICP4 and ICP0; and

(d) total digestion with a BstXI enzyme and then religation to remove sequences beween ICP27 and ICP0.

19. A nucleic acid construct according to claim 15, wherein the viral genomic nucleic acid is from HSV-1 and the viral sequences have been removed from the construct to remove substantially all of the HSV-1 sequences extraneous to ICP0, ICP4, ICP22 and ICP27 coding sequences.

20. A nucleic acid construct according to claim 1, wherein the viral genomic nucleic acid corresponds to a contiguous region of the viral genome it is derived from apart from the replacement of the coding sequences the endogenous gene expression regulatory units are naturally operably linked to with the heterologous coding sequences.

21. A nucleic acid construct according to claim 1, wherein the

endogenous gene expression regulatory units operably linked to the heterologous coding sequences are endogenous promoters.

22. A method of generating a nucleic acid construct for direct administration to a subject to elicit an immune response in the subject, the method comprising:

(a) inserting viral genomic nucleic acid into a vector backbone, said viral genomic nucleic acid comprising at least two endogenous gene expression regulatory units which each comprise an endogenous promoter capable of expression in a mammalian cell, where the endogenous promoters of the units are active at the same phase in the viral cycle of the virus the viral genomic nucleic acid is derived from; and

(b) either prior to, at the same time, or subsequent to inserting the viral genomic nucleic acid into the vector backbone, operably linking each of the endogenous promoters of at least two of the gene expression regulatory units in the viral genomic nucleic acid to heterologous coding sequences

wherein the viral genomic nucleic acid is from 1 to 50 kb in length excluding the heterologous sequences inserted into it.

23. A method according to claim 22, wherein the method further comprises deleting from the viral genomic nucleic acid some or all of the viral sequences, apart from the at least two endogenous gene expression regulatory units, which are present in the region of the viral genome corresponding to that between the 5' and 3' ends of the viral genomic nucleic acid of the construct.

24. A method according to claim 23, wherein the deleted sequences are some or all of the non-coding intervening sequences between adjacent endogenous gene expression regulatory units to which the heterologous coding sequences are to be operably linked.

25. A method according to claim 22, wherein the genomic nucleic acid is inserted into the vector backbone as a single fragment.

26. Coated particles, suitable for delivery from a particle-mediated delivery device, which particles comprise carrier particles coated with a nucleic acid

construct wherein the construct comprises viral genomic nucleic acid, said viral genomic nucleic acid comprising at least two endogenous gene expression regulatory units which each comprise an endogenous promoter capable of expression in a mammalian cell, where the endogenous promoters of the units are active at the same point in the viral cycle of the virus the viral genomic nucleic acid is derived from, where:

- at least two of the endogenous gene expression regulatory units comprising gene expression regulatory units comprising promoters are each operably linked to a heterologous coding sequence inserted into the viral genomic nucleic acid; and
- the viral genomic nucleic acid is from 1 to 50 kb in length excluding the heterologous sequences inserted into it.

27. Coated particles according to claim 26, wherein the carrier particles are gold or tungsten.

28. A dosage receptacle for a particle mediated delivery device comprising coated particles according to claim 26.

29. A particle mediated delivery device loaded with coated particles according to claim 26.

30. A particle mediated delivery device according to claim 29 which is a needleless syringe.

31. A method of obtaining expression in a mammalian cell of a polypeptide of interest, which method comprises transferring into said cells a nucleic acid construct comprising viral genomic nucleic acid, said viral genomic nucleic acid comprising at least two endogenous gene expression regulatory units which each comprise an endogenous promoter capable of expression in a mammalian cell, where the endogenous promoters of the units are active at the same phase in the viral cycle of the virus the viral genomic nucleic acid is derived from, where:

- at least two of the endogenous gene expression regulatory units comprising promoters are each operably linked to a heterologous coding sequence inserted into the viral genomic nucleic acid; and

- the viral genomic nucleic acid is from 1 to 50 kb in length excluding the heterologous sequences inserted into it.

32. A method according to claim 31, wherein the construct is delivered directly into a subject.

33. A method according to claim 32, wherein the construct is delivered by injection, transdermal particle delivery, inhalation, topically, orally, intranasally or transmucosally.

34. A method according to claim 32, wherein the construct is delivered by needleless injection.

35. A method according to claim 34, wherein the nucleic acid construct is coated onto carrier particles.

36. A method of nucleic acid immunisation comprising administering to a subject an effective amount of coated particles, which particles are suitable for delivery from a particle-mediated delivery device, the particles comprising carrier particles coated with a nucleic acid construct, wherein the construct comprises viral genomic nucleic acid, said viral genomic nucleic acid comprising at least two endogenous gene expression regulatory units which each comprise an endogenous promoter capable of expression in a mammalian cell, where the endogenous promoters of the units are active at the same phase in the viral cycle of the virus the viral genomic nucleic acid is derived from, where:

- at least two of the endogenous gene expression regulatory units comprising promoters are each operably linked to a heterologous coding sequence inserted into the viral genomic nucleic acid; and

- the viral genomic nucleic acid is from 1 to 50 kb in length excluding the heterologous sequences inserted into it.

37. A method of generating a nucleic acid construct for direct administration to a subject to elicit an immune response in the subject, the method comprising:

(a) inserting viral genomic nucleic acid into a vector backbone, said viral genomic nucleic acid comprising at least two endogenousgene expression

regulatory units which each comprise an endogenous promoter capable of expression in a mammalian cell, where the endogenous promoters of the units are active at the same phase in the viral cycle of the virus the viral genomic nucleic acid is derived from; and

(b) either prior to, at the same time, or after inserting the viral genomic nucleic acid into the vector backbone, deleting from the viral genomic nucleic acid some or all of the viral sequences, apart from the at least two endogenous gene expression regulatory units, which are present in the region of the viral genome corresponding to that between the 5' and 3' ends of the viral genomic nucleic acid of the construct

where the length of the viral genomic nucleic acid inserted into the vector backbone being from 1 to 50 kb.

38. A method according to claim 37, wherein the nucleic acid sequences deleted are part or all of the non-coding intervening sequences between two of the endogenous promoters.

39. Coated particles, suitable for delivery from a particle-mediated delivery device, which particles comprise carrier particles coated with a nucleic acid construct generated by a method as defined in claim 36.

40. A dosage receptacle for a particle mediated delivery device comprising coated particles according to claim 39.

41. A particle mediated delivery device loaded with coated particles according to claim 40.

42. A method of obtaining expression in a mammalian cell of a polypeptide of interest, which method comprises transferring into said cells a nucleic acid construct generated by a method according to claim 37.

43. A method of nucleic acid immunisation comprising administering to a subject an effective amount of coated particles, which particles are suitable for delivery from a particle-mediated delivery device, the particles comprising carrier particles coated with a nucleic acid construct generated by a method according to claim 37.

44. Use of a nucleic acid construct according to any one of claims 1 to 21, a nucleic acid construct generated by a method according to any one of claims 22 to 25, 37 and 38 or coated particles according to any one of claims 26, 27, and 39 in the manufacture of a medicament for use in nucleic acid immunisation.

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